Comparison and Evaluation of Sensitivity Analysis Methods for Probabilistic Risk Assessments

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Outline

- Why Sensitivity Analysis is Useful
- Identification of Sensitivity Analysis Methods
- Modeling Testbed
- Example Results and Insights
- Comparison
- Recommendations

Key Questions Answered by Sensitivity Analysis

- Sensitivity analysis can answer the following key questions:
  - » What is the impact of changes in input values on model output?
  - » How can variation in output values be apportioned among model inputs?
  - » What are the ranges of inputs associated with best/worst outcomes?
  - » What are the key controllable sources of variability?
  - » What are the critical limits (e.g., emission reduction target for a risk management strategy)?
  - » What are the key contributors to the output uncertainty?

Research Background: Comparison and Evaluation of Sensitivity Analysis Methods for Food Safety Risk Models

- June 2001 workshop to review sensitivity analysis methods and recommend specific criteria for evaluation of methods
- Applied approximately one dozen sensitivity analysis methods to multiple food safety risk assessment models:
  - » *Vibrio Paraheamolyticus*
  - » *Listeria monocytogenes* in Ready-to-Eat foods
  - » *E. coli O157:H7* in ground beef
- Publication of literature review and “white papers” as a special section of *Risk Analysis* (June 2002)
- March 2003 workshop to review results and propose priorities for development of a guidance document for practitioners
- Report on evaluation of methods (www.ce.ncsu.edu/risk)
- Guidance on use of methods (www.ce.ncsu.edu/risk)

Research Background: Comparison and Evaluation of Sensitivity Analysis Methods for Exposure Models

- Based on results for food safety risk models, identified seven of the most practical or powerful sensitivity analysis
- Evaluated their applicability to exposure models based on case studies with a simplified Stochastic Human Exposure and Dose Simulation (SHEDS) model
- Two draft final reports by Mokhtari and Frey
  - www4.ncsu.edu/~frey/
  - Volume 1: Review of Available Methods for Conducting Sensitivity and Uncertainty Analysis in Probabilistic Models
  - Volume 2: Evaluation and Recommendation of Methodology for Conducting Sensitivity Analysis in Probabilistic Models
- Journal paper:
  - Mokhtari, A., H.C. Frey, and J. Zheng, "Evaluation and recommendation of sensitivity analysis methods for application to Stochastic Human Exposure and Dose Simulation (SHEDS) models," *Journal of Exposure Science and Environmental Epidemiology*, 16(6):491-506 (Nov 2006)

Application of Sensitivity Analysis Methods to a Probabilistic Environmental Human Exposure Model

- Objectives:
  - » To evaluate selected sensitivity analysis methods based on practical case studies with a complex model
  - » To present and interpret sensitivity analysis results in a probabilistic framework that includes a temporal dimension

Examples of Sensitivity Analysis Methods for Probabilistic Models

- Nominal range sensitivity analysis
- Differential sensitivity analysis
- **Pearson or Spearman correlation coefficients**
- **Sample or Rank regression analysis**
- **Analysis of variance**
- Classification and regression tree
- **Fourier Amplitude Sensitivity Test**
- **Sobol’s Method**
- Response Surface
- Mutual Information Index
- Scatter plots
- Conditional sensitivity analysis

Key Characteristics of the SHEDS-Pesticides Model

- Simplified SHEDS model used as a testbed
- Based on the SHEDS-Pesticides model
  - Non-linearity and interactions between inputs
  - Saturation points
  - Different input types (continuous versus categorical)
  - Aggregation and carry-over effects
  - Inputs with different sampling time scales (e.g., monthly versus daily inputs)

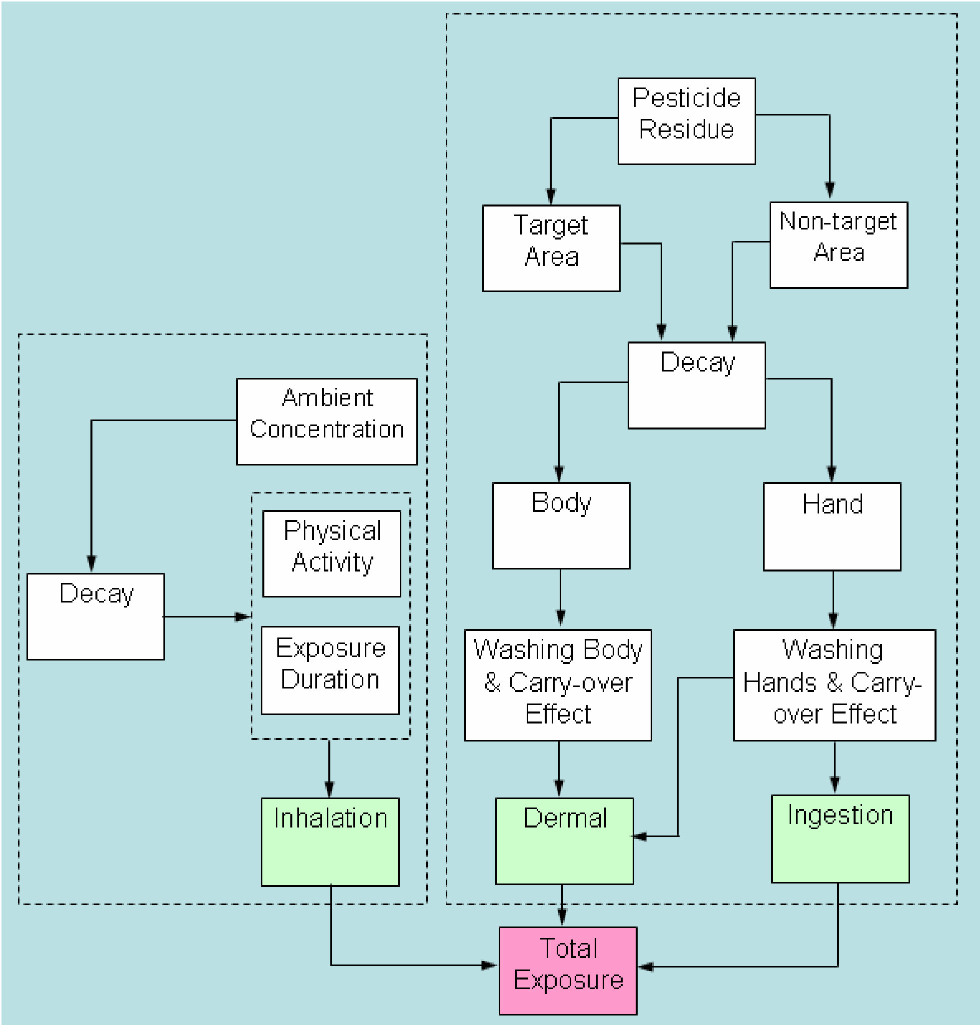
Scenario Assumptions for the Simplified SHEDS-Pesticides Model

- One-stage Monte Carlo simulation
- Inter-individual variability
- Exposure duration of one month
- One application of pesticides at the beginning of the month
- Randomly generated exposure times corresponding to different pathways

Case Study Scenario

- Inter-individual variability in exposures
- Children between 5 and 10
- Total exposure from inhalation, ingestion, and dermal routes
- Three temporal scenarios:
  - Scenario I: Daily total exposure
  - Scenario II: Rate of change of exposure from one day to the next
  - Scenario III: Cumulative Exposure

Schematic Diagram of the Simplified SHEDS-Pesticides Model



Example input Assumptions for the Simplified SHEDS-Pesticides Model: Inhalation Pathway

Inputs	Comments	Distribution	Units	Time Scale
C_{air}	Ambient Concentration of Applied Pesticides	Triangular (0.1,1.0,4.0)	$\mu g/m^3$	monthly
C_b	Background Air Concentration	Lognormal (6.8×10^{-4},1.87)	$\mu g/m^3$	monthly
D_{inh}	Inhalation Exposure Duration	Normal(550,140)	min	daily
PAI	Physical Activity Index	Normal(1.75,0.2)	kcal/kg/day	daily
k	Decay Rate for Pesticides Concentration	Tringular(0.05,0.13,0.40)	1/day	monthly
W_B	Body Weight	Lognormal(30,1.3)	kg	monthly

26 probabilistic inputs in total

Model Application

- Each sensitivity analysis method applied to each time step (i.e., day)
- Ranking - comparative order of importance of an input on a given day when sorted according to sensitivity indices
- Rank = “1” for input with the highest sensitivity index

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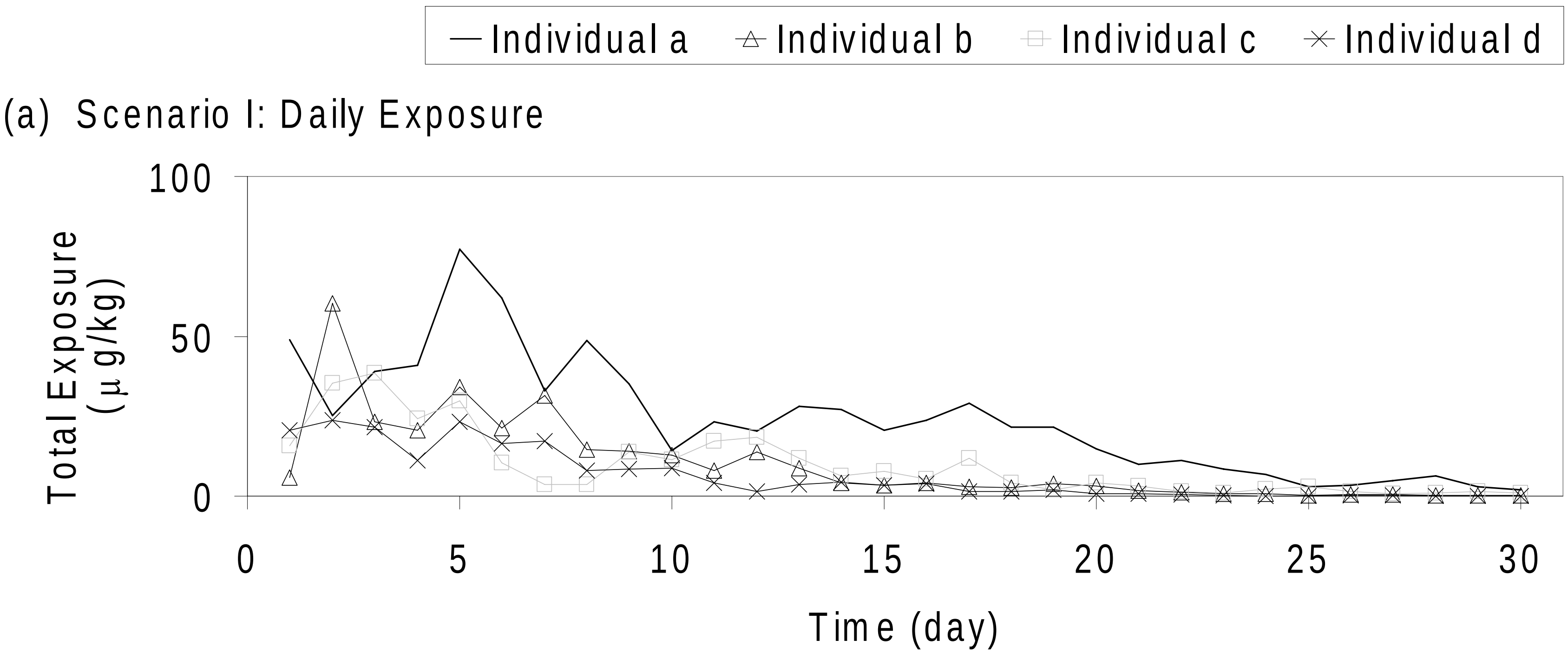
Example Model Output: Daily Exposure for Selected Individuals



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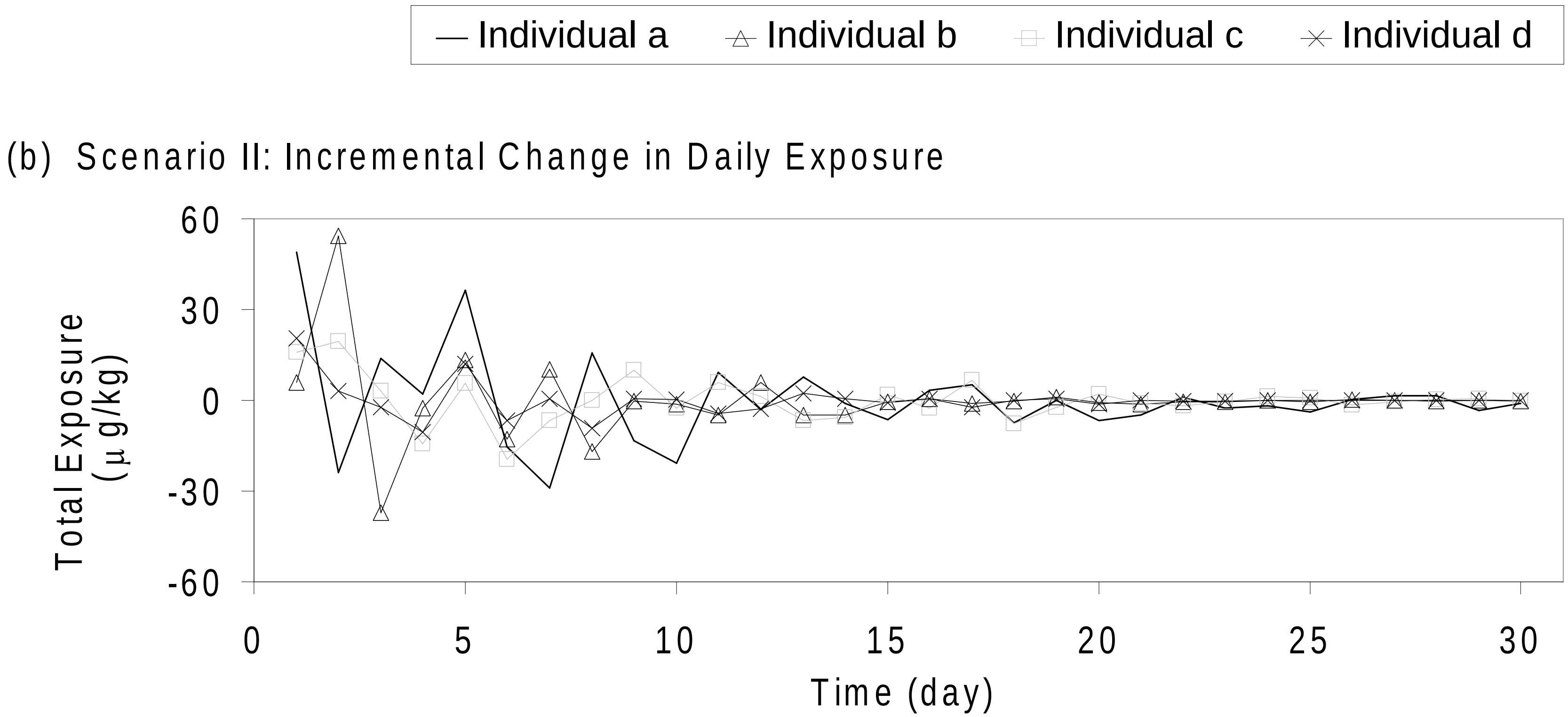
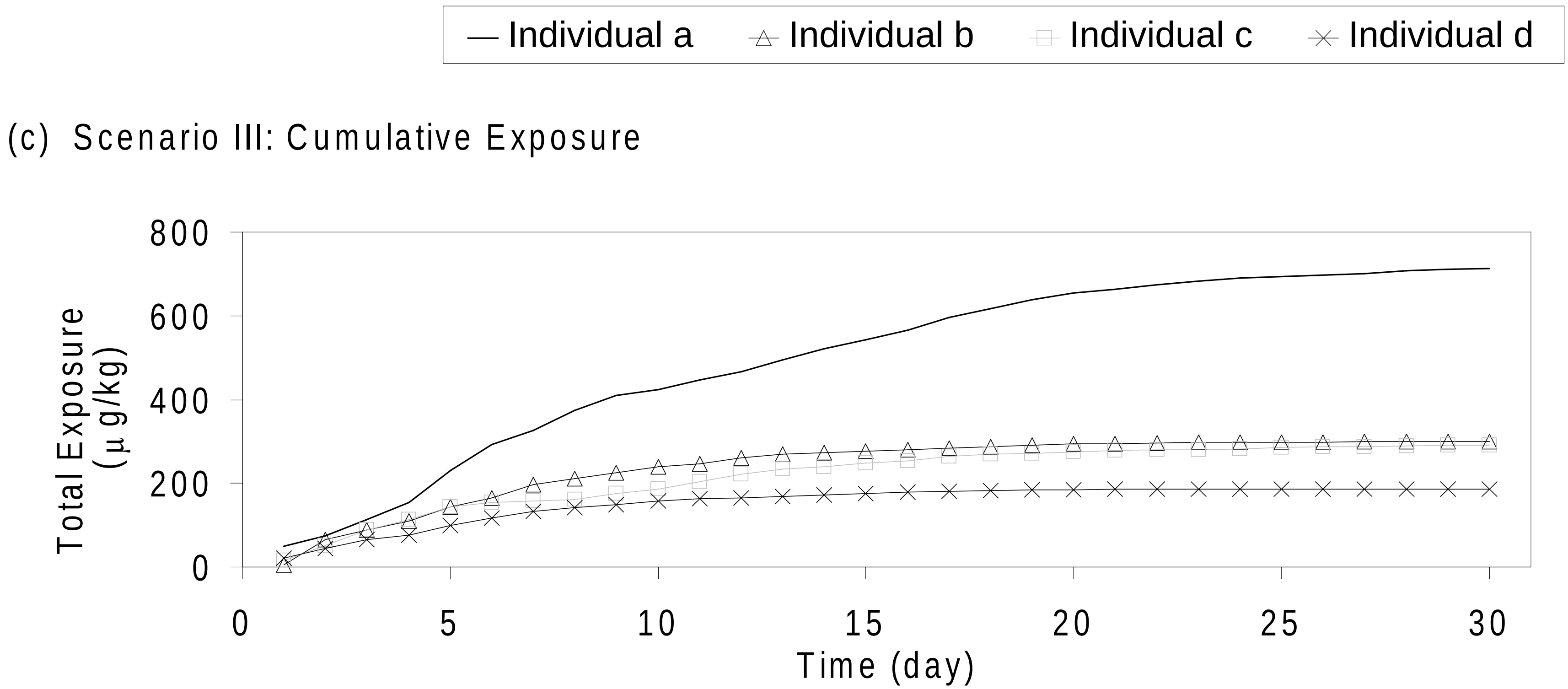
Example Model Output: Incremental Change in Daily Exposure for Selected Individuals



Example Model Output: Cumulative (Temporal) Exposure for Selected Individuals



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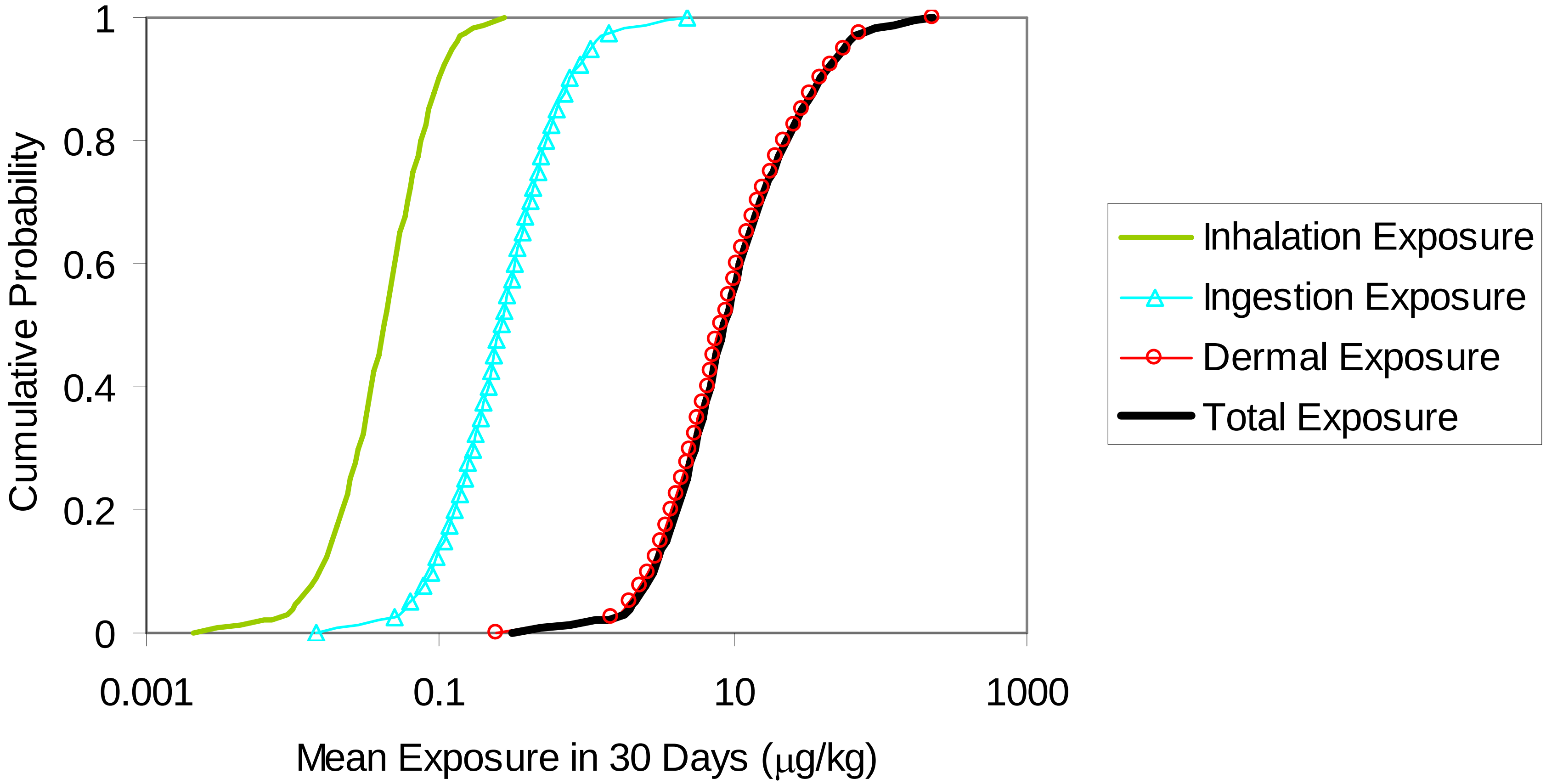
Example Model Output: Inter-Individual Variability in Exposure Over 30 Days



Pearson and Spearman Correlation Coefficients

- Pearson - sample
- Spearman - rank
- Applicable to results of a Monte Carlo analysis
- Correlation coefficients can range from -1 to +1

$$r = \frac{\sigma_{XY}}{\sigma_X \times \sigma_Y} = \frac{\sum_{i=1}^{n}(x_i - \bar{x}) \times (y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2 \times \sum_{i=1}^{n}(y_i - \bar{y})^2}}$$

Pearson (Sample) and Spearman (Rank) Correlation Coefficients (continued)

- Advantages:
  - Relatively easy to compute
  - Can be applied to two-dimensional probabilistic frameworks (correlations for variability, correlations for uncertainty)
  - Readily available in many commercial software packages
- Disadvantages:
  - Pearson correlation - inaccurate for nonlinear models
  - Spearman correlation - inaccurate for non-monotonic models
  - Does not capture interactions among multiple inputs

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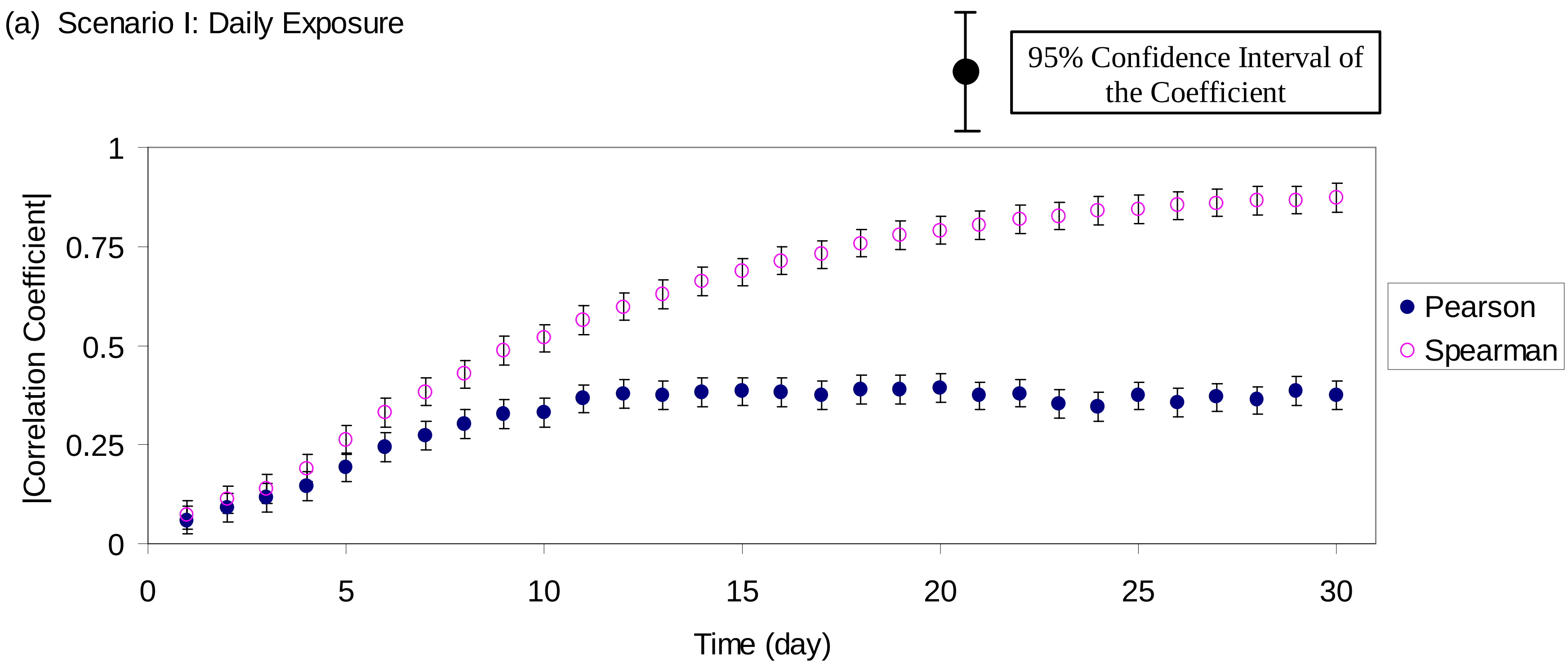
Example Application of Pearson and Spearman Correlation Coefficients to the Simplified SHEDS Model

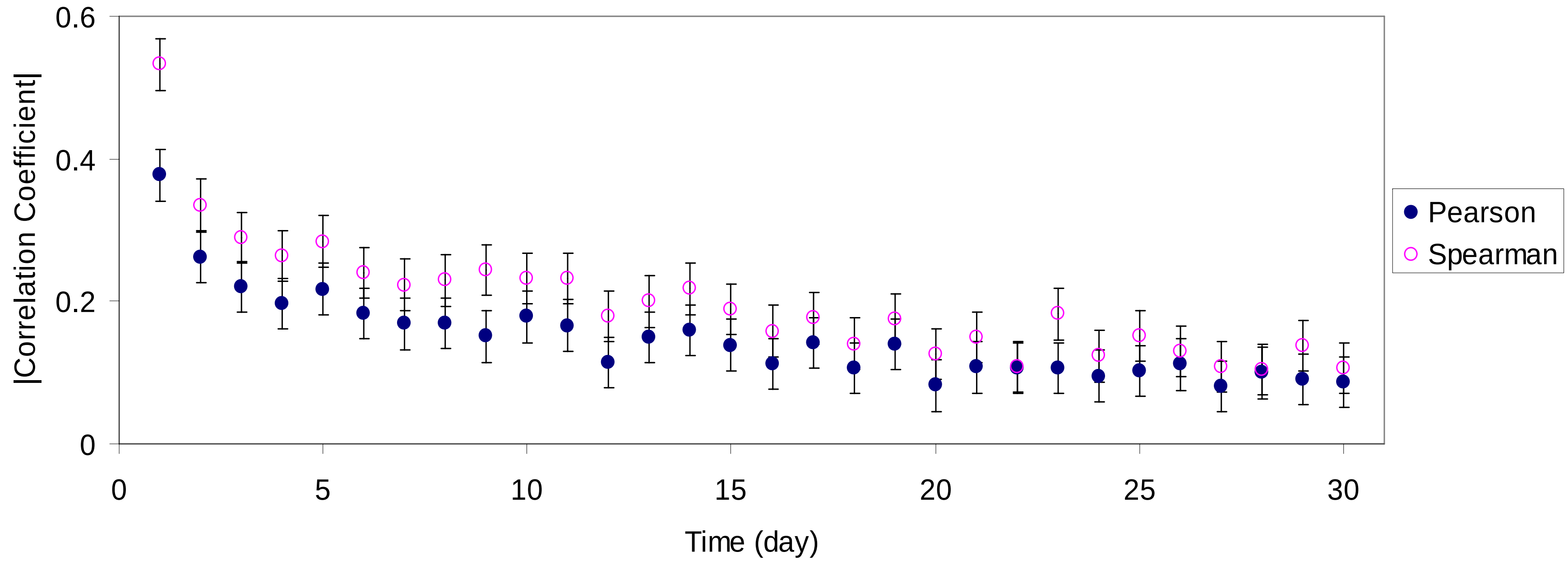


Output: Inter-Individual Variability in Daily Exposure

Input: Residue decay rate (monthly)

Example Application of Pearson and Spearman Correlation Coefficients to the Simplified SHEDS Model

(a) Scenario I: Daily Exposure



Output: Inter-Individual Variability in Daily Exposure

Input: Fraction of Chemicals Available for Transfer (Daily)

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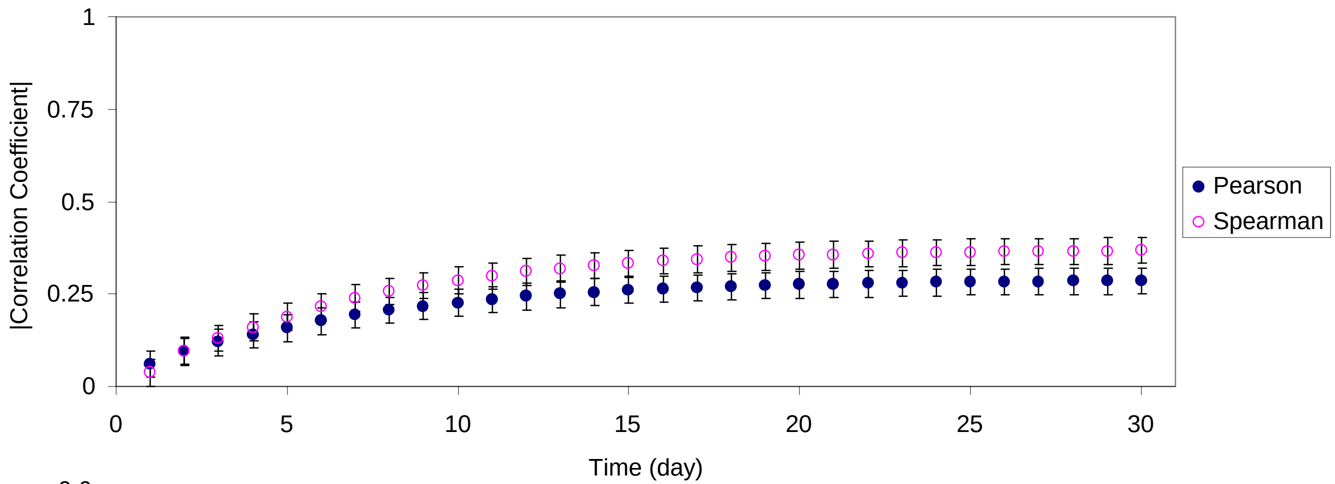
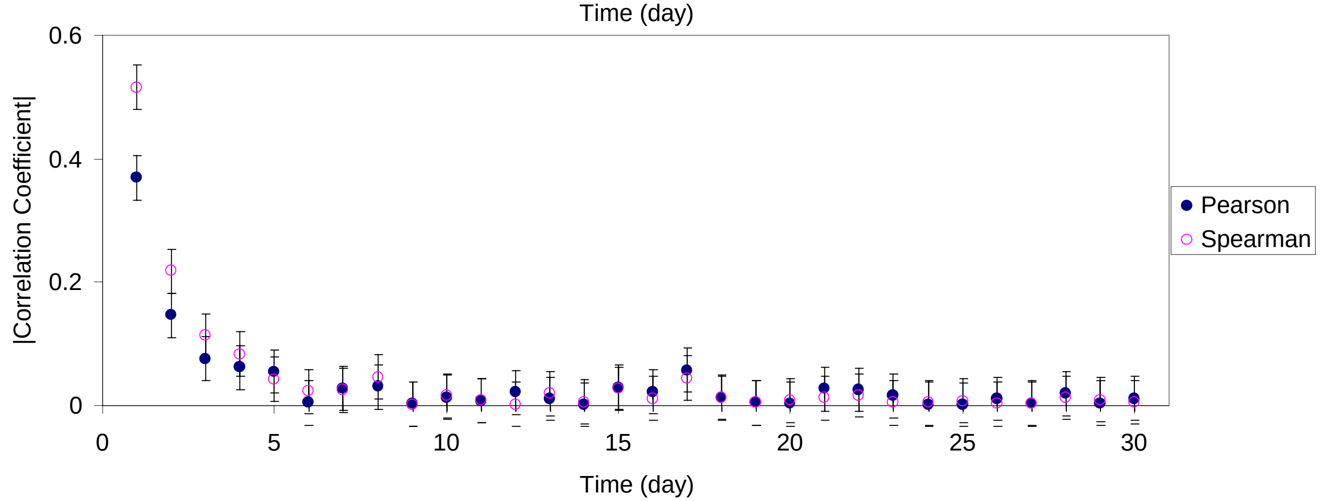
Example Application of Pearson and Spearman Correlation Coefficients to the Simplified SHEDS Model

Input: Residue Decay Rate (Monthly)



Input: Fraction of Chemicals Available for Transfer (Daily)



Output: Inter-Individual Variability in Cumulative Exposure

Fourier Amplitude Sensitivity Test (FAST)

- FAST is a variance-based “global sensitivity analysis” method
- FAST can identify the contribution of individual inputs to the expected value of the output variance
- FAST does not assume a specific functional relationship
- FAST can evaluate sensitivities based on varying only one input or all inputs simultaneously
- FAST provides insights regarding *main* and *total effects* of inputs

Definition of Main and Total Effects

- *Main effect* provides insights regarding contribution of each input to the output variance
- *Total effect* of an input is defined as the sum of all effects involving that input, including interaction effects with other inputs
- Example of *total effect* of X_1 for a case with three inputs:

$$ST_{X_1} = \underbrace{S_{X_1}}_{\text{Main effect of } X_1} + \underbrace{S_{X_1 \times X_2} + S_{X_1 \times X_3} + S_{X_1 \times X_2 \times X_3}}_{\text{Interaction effects involving } X_1}$$

Transformation Functions

- Application of FAST involves defining a set of transformation functions and frequencies for model inputs:

$$x_i = G_i[\sin(\omega_i s)]$$

$$f(x_1, x_2, \ldots, x_n) \rightarrow f(s)$$

i = 1, 2, …, n; n = number of model inputs

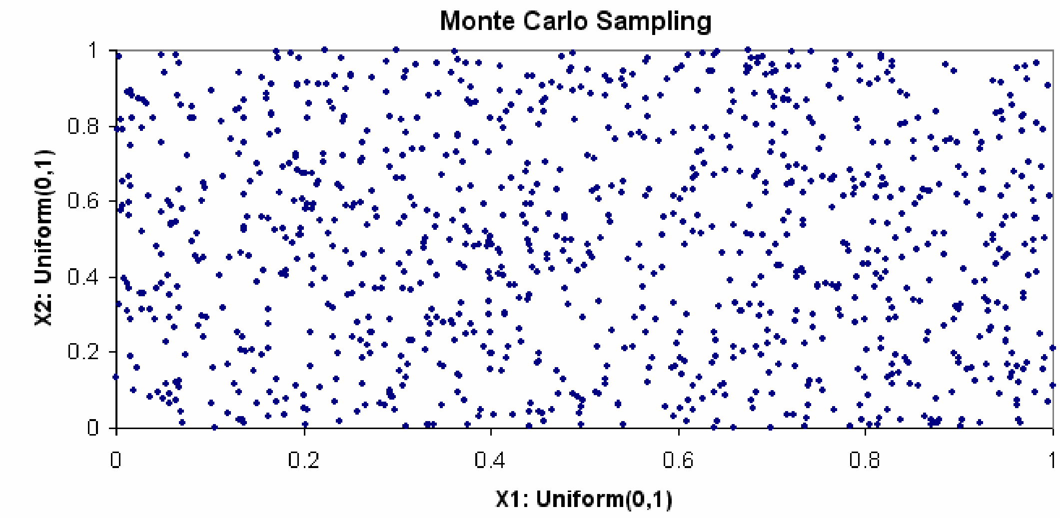
G_i = Transformation function for i^{th} input

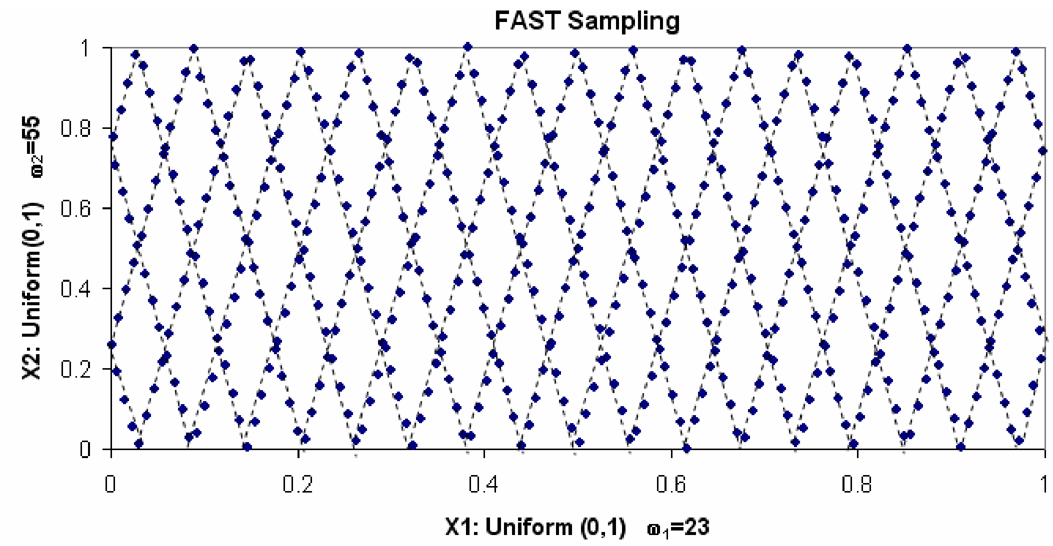
ω_i = frequency for i^{th} input

s = scalar variable

- As *s* varies, all inputs vary simultaneously at rates according to their assigned frequencies
- Frequencies for each input must be distinct and incommensurate

Example of Numerical Samples of Two Uniform Distributions: Monte Carlo vs. FAST





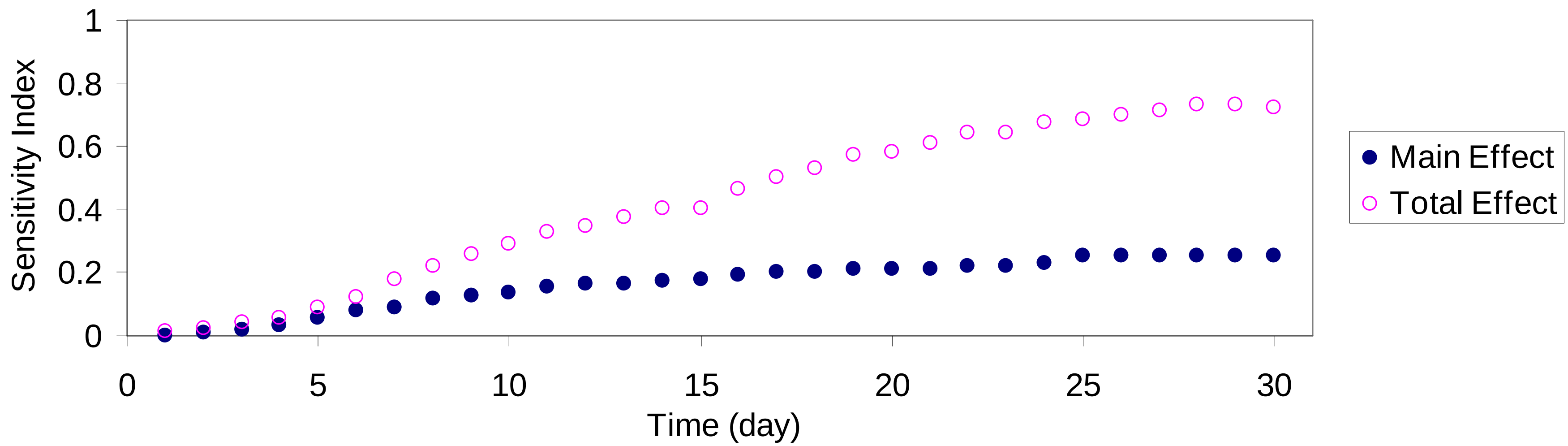
Fourier Amplitude Sensitivity Test (FAST)

(continued)

- Advantages:
  - Model independent
  - Works for monotonic and non-monotonic models
  - The evaluation of sensitivity estimates for each input is based on just a single set of runs
- Disadvantages:
  - Computationally complex
  - Requires an alternative sampling scheme in place of Monte Carlo
  - The reliability of the FAST method can be poor for discrete inputs
  - Current software tools for FAST are not readily amenable to application to the complex risk assessment models

Example Application of FAST to the Simplified SHEDS Model

(a) Scenario I: Daily Exposure



Output: Inter-Individual Variability in Daily Exposure

Input: Residue decay rate (monthly)

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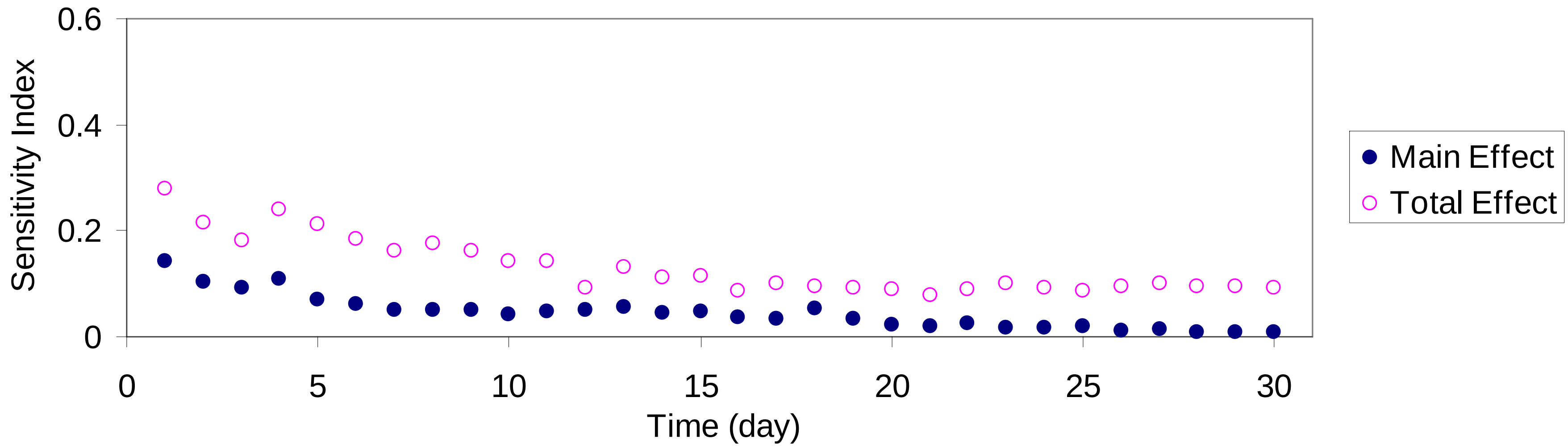
Example Application of FAST to the Simplified SHEDS Model

(a) Scenario I: Daily Exposure



Output: Inter-Individual Variability in Daily Exposure

Input: Fraction of Chemicals Available for Transfer (Daily)

Sobol's Method

- Variance-based "global sensitivity analysis" method
- Contribution of individual inputs to the expected value of the output variance
- Does not assume a specific functional relationship
- *Main effects*, *total effects*, and any order of *interaction effects* for inputs

Sensitivity Indices Based on the Sobol's Method

- A *Monte Carlo* procedure is used for the estimation of the partial variances, and thus, sensitivity indices
- Example sensitivity indices for *main* and *total effects* of inputs:

<u>*Main Effect*</u>

$$S_j = \frac{(\hat{U}_j - \hat{E}^2(y))}{\hat{V}(y)}$$

<u>*Total Effect*</u>

$$ST_j = 1 - \frac{(\hat{U}_{-j} - \hat{E}^2(y))}{\hat{V}(y)}$$

$$\hat{E}(y) = Expected\,Value\,of\;\; y$$

$$\hat{V}(y) = Variance\,of\;\; y$$

The Monte Carlo Procedure for Estimation of Sensitivity Indices

- Two input sample matrices M_1 and M_2 are generated (*n* is the sample size and *k* is the number of inputs):

$$M_1 = \begin{pmatrix} x_{11} & x_{12} & \cdots & x_{1k} \\ x_{21} & x_{22} & \cdots & x_{2k} \\ \vdots & & \ddots & \vdots \\ x_{n1} & x_{n2} & \dots & x_{nk} \end{pmatrix} \qquad M_2 = \begin{pmatrix} x'_{11} & x'_{12} & \cdots & x'_{1k} \\ x'_{21} & x'_{22} & \cdots & x'_{2k} \\ \vdots & & \ddots & \vdots \\ x'_{n1} & x'_{n2} & \dots & x'_{nk} \end{pmatrix}$$

- Parameters in the previous equations are estimated as:

$$\hat{E}^2 = \frac{1}{n}\sum_{r=1}^{n} f(x_{r1}, x_{r2}, \ldots, x_{rk}) \times f(x'_{r1}, x'_{r2}, \ldots, x'_{rk})$$

$$\hat{U}_j = \frac{1}{n-1}\sum_{r=1}^{n} f(x_{r1}, x_{r2}, \ldots, x_{rk}) \times f(x'_{r1}, x'_{r2}, \ldots, x'_{r(j-1)}, x_{rj}, x'_{r(j+1)}, \ldots, x'_{rk})$$

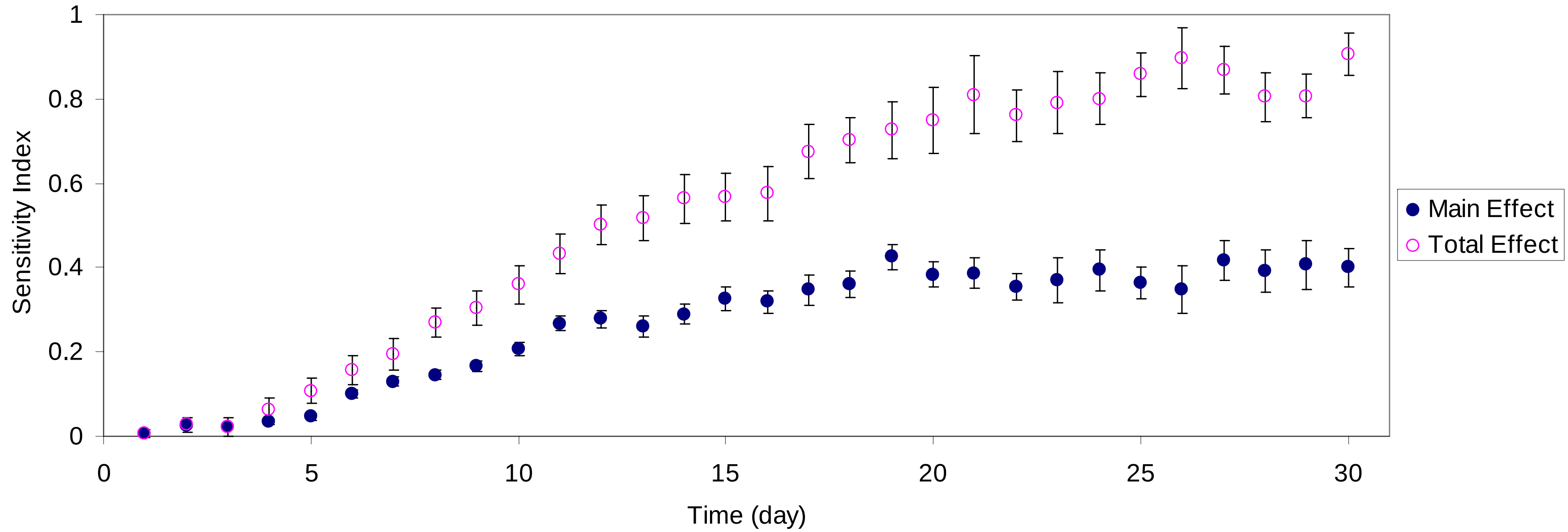
$$\hat{U}_{-j} = \frac{1}{n-1}\sum_{r=1}^{n} f(x_{r1}, x_{r2}, \ldots, x_{rk}) \times f(x_{r1}, x_{r2}, \ldots, x_{r(j-1)}, x'_{rj}, x_{r(j+1)}, \ldots, x_{rk})$$

Sobol's Method (continued)

- Advantages:
  - Sobol's method can cope with both nonlinear and non-monotonic models
  - Sobol's method can be applied to categorical inputs
- Disadvantages:
  - Computationally intensive
  - The ease of application depends on the complexity of the model
  - There is no readily available software that facilitates application of Sobol's method

Example Application of Sobol's Method to the Simplified SHEDS Model

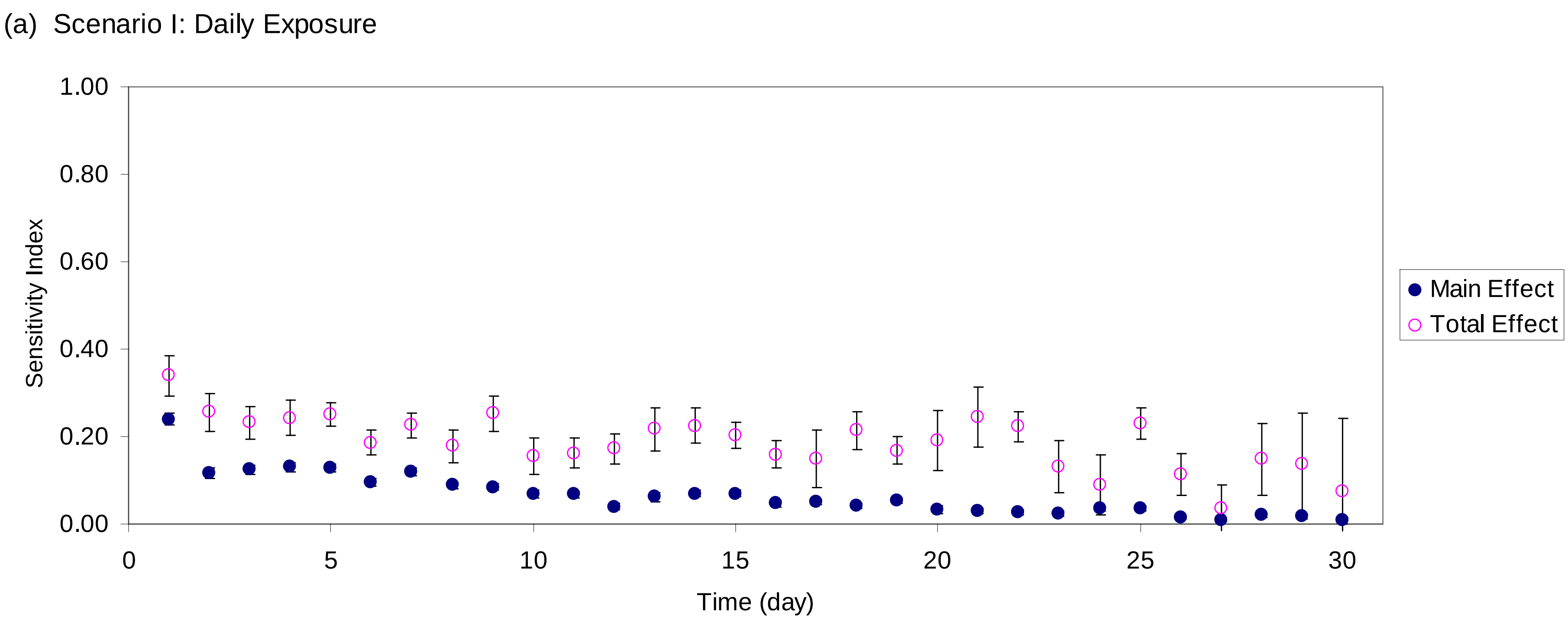
(a) Scenario I: Daily Exposure



Output: Inter-Individual Variability in Daily Exposure

Input: Residue decay rate (monthly)

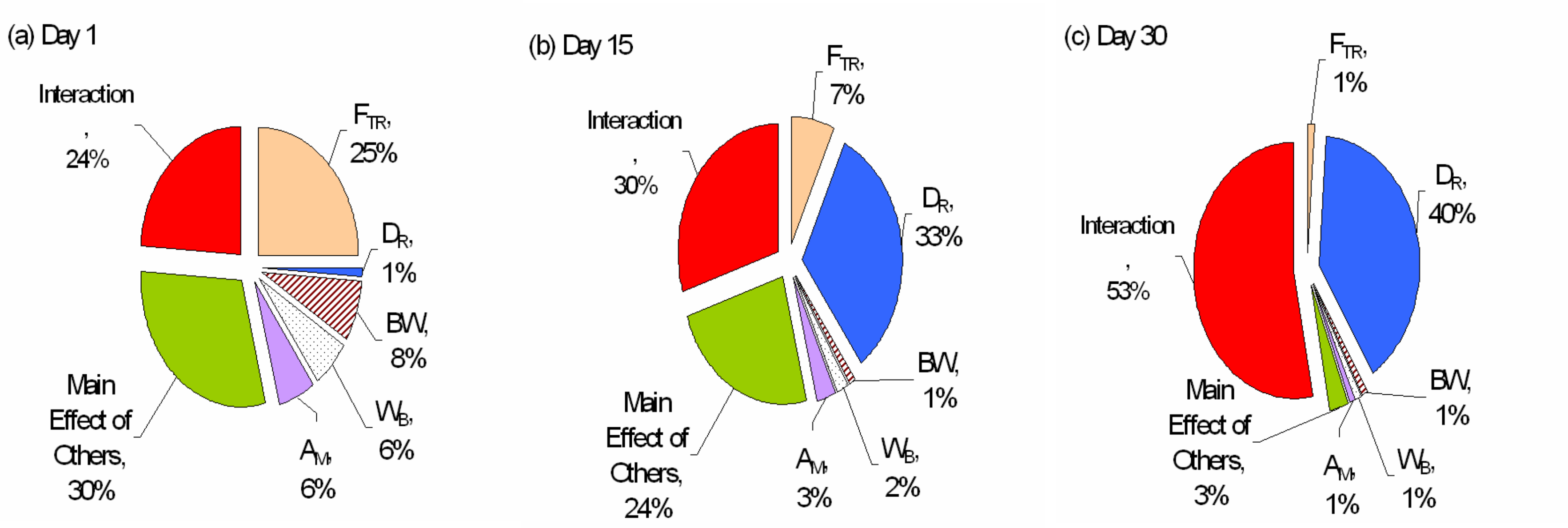
Example Application of Sobol's Method to the Simplified SHEDS Model



Output: Inter-Individual Variability in Daily Exposure

Input: Fraction of Chemicals Available for Transfer (Daily)

Contribution of Inputs to the Output Variance (Scenario I) Based on Sobol's Method



A_M = Mass of applied pesticide

BW = Body washing removal efficiency

D_R = Fraction of pesticides that dissipates daily

F_{TR} = Fraction of pesticide available for transfer from surface to body or hands

W_B = Body weight

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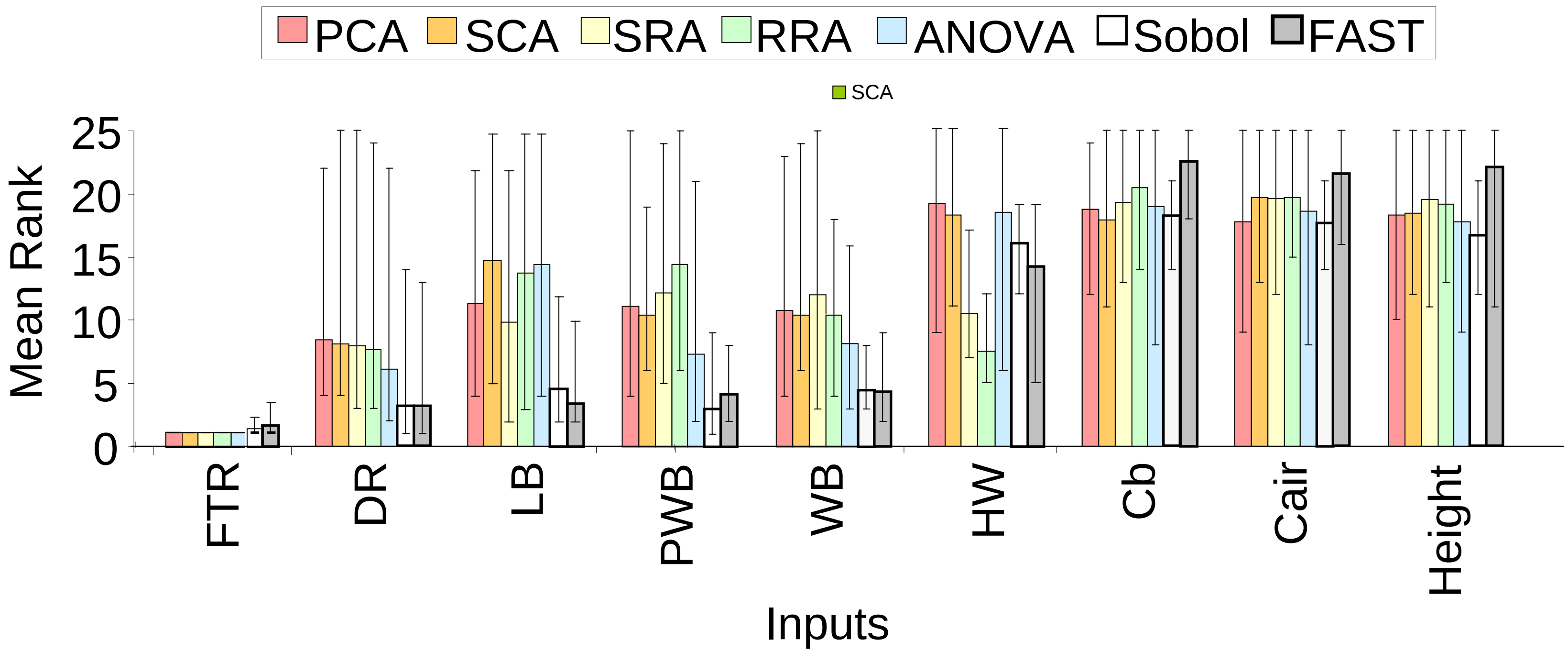
Quantitative Comparison of Sensitivity Analysis Methods for Selected Inputs



FTR = *Fraction of chemicals available for transfer*
DR = *Fraction of residue that dissipates daily*
LB = *Maximum dermal load via body*
PWB = *Probability of washing body*
WB = *Body Weight*
HW = *Hand washing removal efficiency*
Cb = *Background air concentration*
Cair = *Concentration of applied pesticide in air*
Height = *Body height*

Key Findings Based on Comparison of Selected Methods

- Variance-based methods provided lower mean ranks for the most sensitive inputs.
- The range of ranks for each input was typically narrower for the variance-based methods
- All methods provided similar results for insignificant inputs
- Sobol’s method and FAST produced similar rankings, especially for important inputs.

Qualitative Comparison of Sensitivity Analysis Methods

	Sensitivity Analysis Method [a]						
Criteria for Comparison [b]	PCA	SCA	SRA	RRA	ANOVA	FAST	Sobol
Simultaneous Variation in Inputs	++	++	++	++	++	++	++
Computational Efficiency	++	++	++	++	+/-	-	-
Quantitative Measure for Ranking	++	++	++	++	++	++	++
Reproducibility	+/-	+/-	+/-	+/-	+/-	++	+/-
Ability to Apportion the Output Variance	No	No	+/-	+/-	+/-	++	++
Model Independence	No	No	No	No	Yes	Yes	Yes
Ability to deal with interactions	No	No	Yes	Yes	Yes	Yes	Yes
Robustness	+/-	+/-	+/-	+/-	+/-	++	++
Discrete Inputs	-	-	+/-	+/-	++	-	++
Number of Inputs	++	++	++	++	+/-	-	+/-

Conclusions

- Model independent methods are preferable
- Most methods can screen unimportant inputs
- Simple or convenient methods may fail to identify important inputs (e.g., because of interactions)
- Application to “2D” variability and uncertainty is possible (see food safety risk model case studies)
- Sensitivity differs at different time scales, which implies a need to match the time scale of the exposure analysis, sensitivity analysis, and assessment endpoint

Recommendations

- Sobol's method and FAST are attractive methods for apportioning the output variance.
- However, these are computationally intensive.
- Use a tiered approach:
  - a less computationally intensive and more readily available method can be applied for the purpose of determining which inputs are *not* important.
  - Unimportant inputs based on the tiered approach can be set to point estimates.
  - Subsequently, a more computationally intensive but also more accurate method, such as Sobol's method or FAST, can be applied to distinguish among the remaining inputs.

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